RESPONSE

Claims 25-49 are pending. Claims 25 and 26 are amended and claim 34 is cancelled by the present amendment. Claims 39-49 stand withdrawn as drawn to a nonelected invention. Claims 37 and 38 are drawn to nonelected species. Applicants understand that claims 37 and 38 will be examined upon the allowance of a generic claim. Accordingly, claims 25-33 and 35-38 are pending and presented for examination.

Amendments to the Claims

Claim 25 is amended to recite that an antimicrobial coating is on a surface of the article of manufacture. Support for the amendment to claim 25 is found in the originally-filed application at least, for example, on page 4 and in original claim 11.

Claim 26 is amended to delete unnecessary language.

Accordingly, Applicants submit that the amendments to the claims introduce no new matter.

Amendments to the Specification

The specification is amended to correct typographical errors. Applicants submit that the amendments to the specification introduce no new matter.

Rejections under 35 U.S.C. § 112, second paragraph

Claims 25-34 stand rejected under 35 U.S.C. § 112, second paragraph, as allegedly being incomplete for omitting an explicit recitation of a base or surface on which the coating resides. Applicants have amended independent claim 25 to recite that an antimicrobial coating is on a surface of the article of manufacture, and request reconsideration and withdrawal of the rejection.

Claims 26-36 stand rejected under 35 U.S.C. § 112, second paragraph, as allegedly being indefinite. Specifically, the Office action alleges that the term "derivatives" is indefinite. Applicants have amended claim 36 to remove the reference to "derivatives." The Office action also alleges a lack of antecedent basis for the word "surface" in claim 34.

Applicants have amended claim 25, from which claim 34 depends, to recite a surface, thereby providing explicit antecedent basis. Applicants request reconsideration and withdrawal of these rejections.

The Office action inquires whether the compound of claim 33 is correctly spelled, and requests an official name and structure of the N,N-methylene-bis-diglycidylaniline compound. Applicants submit that, although the compound is correctly spelled, other names for the compound are also known. For example, in Example 1(a), the application discloses that this compound is available from Aldrich Chemical Company of Milwaukee, WI. Applicants enclose as Exhibit A a page from an Aldrich catalog, listing the compound as 4,4'-Methylenebis(*N,N*-diglycidylaniline) and providing the chemical structure of the compound near the bottom of the page above Aldrich number 41,280-5. Similarly, page 40 of International Application Number PCT/US94/14636, incorporated by reference into the present application at page 1 under Related Applications, describes the compound as 4,4'-methylene-bis(N,N-diglycidylaniline). See International Publication Number WO 95/17152 (a copy of which is enclosed as Exhibit B) at page 40.

Rejections under 35 U.S.C. § 112, first paragraph

Claim 34 stands rejected under 35 U.S.C. § 112, first paragraph. Applicants have cancelled claim 34 without prejudice solely to expedite prosecution of this application. Accordingly, Applicants request reconsideration and withdrawal of the rejection.

Claims 25-35 stand rejected under 35 U.S.C. § 112, first paragraph, as allegedly claiming subject matter beyond the scope of the specification. Specifically, the Office action alleges that "[h]ow one can arrange no leaching, yet have a microbe take up the metal is not evident." Applicants respectfully traverse this rejection.

The specification discusses, at length, properties of the nitrogen-containing polycationic polymer matrix that promote selective transfer of the antimicrobial metallic material to a contacting organism, thereby providing antimicrobial activity without releasing biocidal amounts of elutables into the surrounding environment. More specifically, the polymer matrix should be immobilizable on a surface. See, e.g., the application as filed, at

page 5. The polymer matrix should reversibly bind or complex with the antimicrobial metal. See id. The association between the polymer matrix and the antimicrobial metal should be strong enough to prevent release of biocidal amounts of the antimicrobial metal into the surrounding environment. See id. Nevertheless, the polymer should not bind the metal so strongly that a contacting microorganism cannot effectively compete for binding to the metal. See id. Transfer of the antimicrobial metal to the microorganism also can be facilitated by using a polycationic polymer matrix capable of insinuating the antimicrobial metal into the cell membrane of an organism. See id.

The specification provides numerous examples of appropriate nitrogen-containing polycationic polymer matrices and antimicrobial metallic materials. Thus, for example, matrices incorporating benzalkoniumchloride derivatives, α-4-[1-tris(2-hydroxyethyl) ammonium-2-butenyl] poly[l-dimethylammonium-2-butenyl]-ω-tris(2-hydroxyethyl) ammonium chloride, and biguanide compounds such as chlorhexidine or polyhexamethylene biguanide are appropriate. See id. at page 18. More generally, the matrix preferably includes a surface active agent to promote penetration of at least the outer portion of the lipid bilayer membrane of a microorganism. See id. at page 6. The matrix should have an appropriate affinity for an antimicrobial metallic material, such as silver, zinc, copper, *etc*. See id. at page 7. The application discloses a wide variety of methods of immobilizing the complex on a surface. See, e.g., id. at pages 8-9.

Applicants submit that it is well within the level of skill in the art to identify a surface active agent and to measure or ascertain from the literature an affinity constant for a polymer (or for a specific functional group thereof) and a metal. From the affinity constant, one of ordinary skill in the art can deduce whether biocidal amounts of the antimicrobial metallic material would be released into the surrounding environment. The affinity constant also can be compared to the affinity constant of the antimicrobial metallic material for the molecules (*e.g.*, proteins) of a target microorganism to determine whether any appreciable transfer of the antimicrobial metallic material to the target microorganism would occur.

In view of the extensive teachings in the specification regarding chemical properties useful for preparing the antimicrobial coatings, the numerous examples of appropriate

materials for incorporation into the coatings, the level of skill in the art, and the many examples (on pages 29-42 of the application as filed) of tests confirming antimicrobial activity and nonrelease of biocidal amounts of elutables into the surrounding environment, Applicants submit that the practice of the full scope of the claims would not require undue experimentation. Accordingly, Applicants request reconsideration and withdrawal of the rejection.

Obviousness-type double patenting rejections

Claims 25-34 stand rejected under the judicially created doctrine of obviousness-type double patenting as allegedly unpatentable over claims 1-6 of U.S. Patent No. 5,849,311. Claims 25, 27, 28, and 31-34 also stand rejected over claims 1-9 of U.S. Patent No. 5,817,325. In accordance with 37 C.F.R. § 1.111(b), Applicants request that the double patenting rejections be held in abeyance until otherwise-allowable subject matter is indicated.

Rejections under 35 U.S.C. § 102

Claims 25, 27, 28, 31 and 34-36 stand rejected under 35 U.S.C. § 102(b) as allegedly being anticipated by U.S. Patent No. 4,592,920 to Murtfeldt ("Murtfeldt"). Applicants respectfully traverse this rejection.

Murtfeldt does not disclose a coating comprising a nitrogen-containing polycationic polymer matrix. The Office action notes that Murtfeldt teaches use of a polyurethane "suspending agent" (Murtfeldt at column 3, lines 50-54). Polyurethanes are not necessarily polycationic: some are described in the art as anionic, others as cationic, and still others as nonionic. See, e.g., www.lamberti.com/technologies/Polyurethane.cfm, a copy of which is attached as Exhibit C, describing various polyurethanes as "anionic," "cationic," or "non ionic." See also U.S. Patent Nos. 3,951,897 and 4,180,491 (copies of which are enclosed as Exhibits D and E), referring to "nonionic" polyurethanes. Murtfeldt does not teach that its polyurethane is or should be polycationic. Accordingly, Murtfeldt does not disclose an antimicrobial coating comprising a nitrogen-containing polycationic polymer matrix and does

not anticipate the pending claims. Applicants therefore request reconsideration and withdrawal of the rejection.

Claims 25-28, 30-32, and 34-36 stand rejected under 35 U.S.C. § 102(b) as allegedly anticipated by U.S. Patent No. 5,019,096 to Fox, Jr., *et al.* ("Fox"). Applicants respectfully traverse this rejection.

Fox fails to teach a "coating that does not release biocidal amounts of elutables into the surrounding environment" as required by the pending claims. Indeed, Fox teaches the opposite: a layer that permits controlled release of biguanide and silver ions from the matrix over time. See Fox, col. 1, line 64 through col. 2, line 2; col. 3, line 55 through col. 4, line 4, and the claims. The importance in Fox of releasing biocidal materials is underscored both by the disclosure at column 14, lines 20-23 ("the time release matrix system . . . allows for a dose that is . . . effective against microorganisms") and by the generation of a "zone of inhibition," characterizing the biocidal activity of Fox's biocidal materials. See, e.g., Fox, Examples 5, 6, 7, 13, 16, and 24-26). Absent a specific disclosure of the claimed invention, Fox cannot anticipate the pending claims. Applicants therefore request reconsideration and withdrawal of this rejection.

Claims 25, 27, and 34 stand rejected under 35 U.S.C. § 102(a) as allegedly being anticipated by JP 08176527 ("Honda"). Applicants note that claim 34 has been cancelled without prejudice. Applicants respectfully traverse the rejection as applied to claims 25 and 27.

Applicants submit that claims 25 and 27 are entitled to at least a priority date of December 19, 1994, the filing date of International Application Number PCT/US94/14636, to which the present application claims priority under 35 U.S.C. § 120. See, e.g., International Application Number PCT/US94/14636 at the paragraph bridging pages 22 and 23, describing pellets or beads having a combination of an organic antimicrobial agent and an inorganic antimicrobial agent attached or coated on the surface; the preferred organic antimicrobial agents include polycationic compounds such as benzalkonium derivatives and biguanide compounds, and the preferred inorganic antimicrobial agents include elemental silver or silver compounds. A copy of International Publication Number WO 95/17152, which corresponds to International Application Number PCT/US94/14636, is attached as Exhibit B. Accordingly, Applicants

submit that Honda is not available as prior art under 35 U.S.C. § 102(a) against pending claims 25 and 27, and respectfully request reconsideration and withdrawal of the rejection.

Claims 25, 27, and 34 stand rejected under 35 U.S.C. § 102(b) as allegedly being anticipated by JP 05033217 ("Kawamura"). Applicants respectfully traverse this rejection.

Kawamura teaches a modified polyurethane elastic yarn. Like Murtfeldt, Kawamura does not teach that its modified polyurethane is or should be polycationic. Accordingly, Kawamura does not teach an antimicrobial coating comprising a nitrogen-containing polycationic polymer matrix. Because Kawamura does not disclose the claimed invention, Applicants request reconsideration and withdrawal of this rejection.

Claims 25-28, 31, 35 and 36 stand rejected under 35 U.S.C. § 102(b) as allegedly being anticipated by Mermel *et al.* (1993) J. Infect. Dis. 167:920-4 ("Mermel"). As in Fox, Mermel reports antimicrobial activity that leaches from the surface. See, e.g., Mermel at the last row of Table 1, showing antimicrobial activity leaching from the surface to give zones of inhibition effective as far as 11.0 mm from the surface. Because Mermel fails to teach an antimicrobial coating that does not release biocidal amounts of elutables into the surrounding environment, Mermel does not anticipate the claimed invention. Accordingly, Applicants request reconsideration and withdrawal of this rejection.

CONCLUSION

Claims 25-33 and 35-38 are pending and presented for examination. Based on the amendments and remarks presented above, Applicants submit that these claims are in condition for allowance and respectfully request entry as such. The Examiner is encouraged to call the undersigned to discuss any outstanding issues related to this application.

Respectfully submitted,

Date: December 5, 2002
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Version with markings to show changes made

Amendments to the claims

25. (Amended) An article of manufacture comprising an antimicrobial coating on a surface of the article of manufacture, wherein the antimicrobial coating comprises a nitrogen-containing polycationic polymer matrix having dispersed therein or attached thereto an antimicrobial metallic material such that the antimicrobial coating does not release biocidal amounts of elutables into the surrounding environment.

26. (Amended) The article of claim 25 wherein the nitrogen-containing polycationic polymer matrix comprises benzalkonium groups [or derivatives thereof].

Amendments to the Specification

Preferred cationic materials include benzalkoniumchloride derivatives, [a-4-[1-tris(2-hydroxyethyl) ammonium-2-butenyl] poly[l-dimethylammonium-2-butenyl]-ω -tris(2-hydroxyethyl) ammonium chloride] α-4-[1-tris(2-hydroxyethyl) ammonium-2-butenyl] poly[l-dimethylammonium-2-butenyl]-ω-tris(2-hydroxyethyl) ammonium chloride, and biguanides of the general formula:

$$Y_1\text{-}[\text{-NH-C(=NH)-NH-C(=NH)-NH-X-}]_n\text{-}Y_2$$

or their water soluble salts, where X is any aliphatic, cycloaliphatic, aromatic, substituted aliphatic, substituted aromatic, heteroaliphatic, heterocyclic, or heteroaromatic compound, or a mixture of any of these, and Y_1 and Y_2 are any aliphatic, cycloaliphatic, aromatic, substituted aliphatic, substituted aromatic, heteroaliphatic, heterocyclic, or heteroaromatic compound, or a mixture of any of these, and where n is an integer equal to or greater than 1. Preferred compounds include, e.g., chlorhexidine (available from Aldrich Chemical Co., Milwaukee, WI) or polyhexamethylene biguanide (available from Zeneca Biocides, Inc. of Wilmington, DE). The above-mentioned organic materials may be modified to include a thiol group in their structure so as to allow for the bonding of the compound to a metallic substrate, or may be derivatized with

other functional groups to permit direct immobilization on a non-metallic substrate. For example, the above-mentioned organic materials may be suitably functionalized to incorporate groups such as hydroxy, amine, halogen, epoxy, alkyl or alkoxy silyl functionalities to enable direct immobilization to a surface.